

Multiscaling for Classical Nanosystems: Derivation of Smoluchowski & Fokker-Planck Equations

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January 8, 2010

Abstract

Using multiscale analysis and methods of statistical physics, we show that a solution to the N -atom Liouville Equation can be decomposed via an expansion in terms of a smallness parameter ϵ , wherein the long scale time behavior depends upon a reduced probability density that is a function of slow-evolving order parameters. This reduced probability density is shown to satisfy the Smoluchowski equation up to $O(\epsilon^2)$ for a given range of initial conditions. Furthermore, under the additional assumption that the nanoparticle momentum evolves on a slow time scale, we show that this reduced probability density satisfies a Fokker-Planck equation up to $O(\epsilon^2)$. This approach has applications to a broad range of problems in the nanosciences.

Keywords: nanosystems, all-atom multiscale analysis (AMA), Gibbs Hypothesis, Smoluchowski equations, Fokker-Planck equations

1 Introduction

Nanosystems are currently of great interest in the fundamental and applied life sciences. A major unresolved challenge is to develop a predictive approach to these systems that capture the inter-communication among the processes operating on differing scales in space and time. The premise of the present work is that one can introduce order parameters (slowly varying quantities that capture the essence of large-scale bionanosystem phenomena) and then, using Newton's equations for the N -atom system, derive equations for stochastic order parameter dynamics.

Examples of bionanosystems abound in nature and medicine. Viruses are supra-million atom entities with complex structural and functional characteristics, including dramatic transitions, interactions with host cells, and self-assembly of subunits. Ribosomes are of size and complexity similar to viruses, and mediate an important

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intercellular process - translation of mRNA into proteins. Protein nanoviruses conduct electric currents, allowing some bacteria to exploit oxide mineral grains when performing oxidation in the oxygen-poor subsurface. In addition to these natural phenomena, scientists are currently developing nanocapsules for the delivery of therapeutic payloads (such as drugs, siRNA, or genes) to diseased tissues, and for medical imaging by equipping nanoparticles with fluorescent subunits while other subunits are designed to bind with diseased cell membrane-bound proteins. Finally, researchers are designing mutated viruses with diminished virulence to serve as vaccines.

To address all of these applications, one would like to develop predictive modules with the ability to efficiently simulate the dynamics of bionanosystems. Such programs should include the following characteristics :

- an underlying all-atom description to evaluate the interaction of bionanosystems with selected molecules, membranes, or other features in their background microenvironment
- a model that does not require recalibration with each new application
- an approach that builds in the detailed physical molecular laws and the predictive power following from them
- an approach that is computationally feasible.

Considering this list, we suggest that a multiscale analysis of the equations of N -atom physics will fulfill each of these requirements. Molecular Dynamics (MD) is a current state-of-the-art software package that efficiently performs simulations of Newton's equations for each of N atoms in a system of interest. An efficient MD code, NAMD, has previously been used to simulate a whole virus using a 1024 CPU supercomputer, but the process proceeds at a rate of about 1 nanosecond of simulated time per day. The typical timescale for a viral structural transition is on the order of a millisecond or greater. Thus, the aforementioned MD code and hardware would take 3,000 years or longer to attain meaningful results. As bionanosystems evolve due to the cross-talk between processes which take place on many scales in both space and time, a computational algorithm based on a multiscale approach seems like a natural choice.

The use of multiscale techniques in statistical mechanics beginning with the Liouville equation has a long history (see [10], [6], [7], and [11], and more recently [5], [2], and [3]). In the present work, we demonstrate several new elements of the analysis. First, in our approach, the nanoparticle's internal atomic state, as well as that of the microenvironment, are maintained allowing for a more natural, symmetric starting

description. Additionally, we utilize a version of the Gibbs postulated equivalence of ensemble and long-time averages, following classical results within ergodic theory. A precise representation is obtained for the momentum factor in the normalization constant for the lowest-order N -atom probability density in a perturbation expansion of a solution to the Liouville equation. As a result, Fokker-Planck and Smoluchowski equations are derived which describe the stochastic dynamics of these slow-evolving order parameters. These results can then be utilized in the production of an efficient software module that can model nanoparticle behavior over long time scales, thereby capturing the necessary structural dynamics of a virus.

In recent investigations (see [2] and [3]), the reduced probability density W was shown to obey an unconserved equation of Fokker-Planck type up to $O(\epsilon^2)$. The derivation of this equation was inconsistent with the mathematical framework of differential equations as the thermal average and the derivatives with respect to order parameters $\frac{\partial}{\partial \Phi}$ and $\frac{\partial}{\partial \Pi}$ do not commute. In the work that follows, we eliminate ambiguities regarding the permutation of the thermal average and these derivatives. Additionally, the lowest order distribution was previously taken to be independent of the conjugate momentum Π . This is done in error, causing the lowest order dependence on the slow variable Π to be lost and propagating this throughout the multiscale analysis. In Section 3, we rigorously correct these mistakes and establish many of the ideas of [3] on a more precise footing by showing that the correction to the reduced probability density \widetilde{W} indeed satisfies a Fokker-Planck equation in conservative form. Prior to this, we show in Section 2 that if the momentum is an atomically varying quantity, rather than a slowly varying order parameter, then \widetilde{W} directly satisfies the Smoluchowski diffusion equation up to $O(\epsilon^2)$. In both sections, our derivations occur from the starting point of the general kinetic equation so that the resulting coarse-grained equations do not arrive from solubility conditions, but from a rational expansion of the Liouville equation.

2 Multiscale Analysis: Smoluchowski Equation

A central goal of multiscale analysis is to rigorously derive coarse-grained equations starting from a more fundamental, final scale theory. The Liouville equation has been a common starting point. The challenge is that while the Liouville equation preserves probability by construction, it is not guaranteed that a given truncation of the equation will be conserving. A re-examination of multiscale analysis for the Liouville equation is now carried out to identify potential difficulties of this type that may arise, and to set forth techniques to resolve them. In this section we resolve probability conservation violations when the momentum is not a slow variable.

Consider the Liouville equation in a multiscale framework wherein order parameters are introduced. We consider an N -atom system consisting of a nanoparticle of

N^* atoms and a host medium of $N - N^*$ atoms. For each atom $i = 1, \dots, N$, we write $p_i, r_i \in \mathbb{R}^3$, and $m_i > 0$ as the momentum, position, and mass of atom i respectively. In addition, we use the notation $\Gamma = \{r_1, p_1, \dots, r_N, p_N\}$. For each $i = 1, \dots, N$, define the indicator function

$$\theta_i = \begin{cases} 1, & \text{if atom } i \text{ is in the nanoparticle} \\ 0, & \text{otherwise.} \end{cases}$$

For the nanoparticle, we define its total mass

$$m = \sum_{i=1}^N m_i \theta_i,$$

the center of mass

$$R = \sum_{i=1}^N \frac{m_i}{m} r_i \theta_i, \quad (1)$$

and the total momentum

$$P = \sum_{i=1}^N p_i \theta_i. \quad (2)$$

To begin the multiscale analysis, we first introduce a dimensionless scaling parameter ϵ in the mass terms by writing

$$\epsilon = \frac{\hat{m}}{m}, \quad (3)$$

where \hat{m} is the mass of a typical atom. In the case that all atoms in the nanoparticle have the same mass, $m_i = \hat{m}$ for all $i = 1, \dots, N^*$, it follows that $\frac{\hat{m}}{m} = \frac{1}{N^*}$. Hence, $\epsilon \approx (N^*)^{-1}$. In this section, we make the following assumptions:

1. The total nanoparticle momentum does not evolve slowly - P is $O(\epsilon^0)$.
2. The net force on the nanoparticle is not decreased due to cancelation of atomic contributions - f is $O(\epsilon^0)$.
3. Large migration distances are not a consideration - R is $O(\epsilon^0)$.

As a result, order parameters are $O(\epsilon^0)$ and need not be scaled in ϵ , even though Newton's equations show that they evolve slowly as $\frac{dR}{dt} = \frac{P}{m} = \epsilon \frac{P}{\hat{m}} = O(\epsilon)$. We note that other scalings would be appropriate to capture different behavioral regimes.

Let us assume ρ satisfies the Liouville Equation

$$\frac{\partial \rho}{\partial t} = - \sum_{i=1}^N \left[\frac{p_i}{m_i} \cdot \frac{\partial}{\partial r_i} + F_i \cdot \frac{\partial}{\partial p_i} \right] \rho \equiv \mathcal{L} \rho \quad (4)$$

where we define F_i to be the force on atom i and t to be time. In addition, we assume throughout that ρ decays at infinity (a standard assumption for a probability density) so that boundary terms do not appear in the calculations from integration by parts. Denote the collection of all atomic positions by $\Gamma_r = \{r_1, \dots, r_N\}$. Given the probability density, $\rho(\Gamma, t)$, we define

$$\widetilde{W}(R, t) = \int \Delta(\Gamma_r^*, R) \rho(\Gamma^*, t) d\Gamma^* \quad (5)$$

where

$$\Delta(\Gamma_r^*, R) = \delta(R - R^*), \quad (6)$$

R is the center of mass order parameter, and

$$R^* = \sum_{i=1}^N \frac{m_i}{m} r_i^* \theta_i$$

is the Γ_r^* -dependent value of R . Then, using the dependence of \widetilde{W} on ρ , a solution to the Liouville equation, we may show that \widetilde{W} must satisfy a conserved equation. Since ρ satisfies (4), we find

$$\begin{aligned} \frac{\partial \widetilde{W}}{\partial t} &= \int \Delta \frac{\partial \rho}{\partial t}(\Gamma^*, t) d\Gamma^* \\ &= - \int \Delta \left(\sum_{i=1}^N \frac{p_i^*}{m_i} \cdot \frac{\partial \rho}{\partial r_i^*} + F_i \cdot \frac{\partial \rho}{\partial p_i^*} \right) d\Gamma^* \\ &= \int \rho \left(\sum_{i=1}^N \frac{p_i^*}{m_i} \cdot \frac{\partial \Delta}{\partial r_i^*} + F_i \cdot \frac{\partial \Delta}{\partial p_i^*} \right) d\Gamma^* \\ &= - \int \rho \left(\sum_{i=1}^N \frac{p_i^*}{m_i} \cdot \frac{\partial R^*}{\partial r_i^*} + F_i \cdot \frac{\partial R^*}{\partial p_i^*} \right) \frac{\partial \Delta}{\partial R} d\Gamma^* \\ &= \frac{\partial}{\partial R} \left(\int \rho \Delta \mathcal{L} R^* d\Gamma^* \right) \\ &= - \frac{\partial}{\partial R} \left(\int \rho \Delta \frac{P^*}{m} d\Gamma^* \right) \end{aligned}$$

Thus, the reduced probability density, \widetilde{W} , satisfies

$$\frac{\partial \widetilde{W}}{\partial t} = -\epsilon \frac{\partial}{\partial R} \left(\int \rho \Delta \frac{P^*}{m} d\Gamma^* \right). \quad (7)$$

Next, we attempt to determine ρ up to $O(\epsilon)$. The N-atom probability density, $\rho(\Gamma, t)$, is then assumed to be expressed as a function of an additional argument, $\Upsilon(\Gamma, t, \cdot)$ in such a way that when the last argument is evaluated at R , ρ is obtained, i.e $\rho(\Gamma, t) = \Upsilon(\Gamma, t, R)$. Instead of labeling this new function, we will just extend our

previous notation and refer to it as $\rho(\Gamma, t, R)$. This displays the dependence of the probability density on multiple scales of motion. Hence, ρ depends on the all-atom descriptive variables Γ , as well as on R defined by (1), the latter an expression of the fact that ρ has indirect dependence on the all-atom state through order parameters and thus depends on the all-atom state in several, distinct ways.

We apply the Liouville operator to $\rho(\Gamma, t, R)$ and invoke the chain rule to find

$$\frac{\partial \rho}{\partial t} = -\mathcal{L}_0 \rho - \sum_{i=1}^N \frac{p_i}{m_i} \cdot \frac{dR}{dr_i} \frac{\partial \rho}{\partial R}.$$

Using (1) this becomes

$$\frac{\partial \rho}{\partial t} = -\mathcal{L}_0 \rho - \frac{P}{m} \cdot \frac{\partial \rho}{\partial R}. \quad (8)$$

Here, we are writing \mathcal{L}_0 instead of \mathcal{L} because these derivatives are taken at constant values of R . By introducing (3) into (8), the Liouville equation (4) transforms into a multiscale equation (see [2] and [3] for more details) as

$$\frac{\partial \rho}{\partial t} = (\mathcal{L}_0 + \epsilon \mathcal{L}_1) \rho \quad (9)$$

where

$$\mathcal{L}_0 = - \sum_{i=1}^N \left[\frac{p_i}{m_i} \cdot \frac{\partial}{\partial r_i} + F_i \cdot \frac{\partial}{\partial p_i} \right] \quad (10)$$

and

$$\mathcal{L}_1 = - \frac{P}{\hat{m}} \cdot \frac{\partial}{\partial R}. \quad (11)$$

Again, it must be noted that \mathcal{L} and \mathcal{L}_0 , while seemingly exact in definition, differ because the differentiation in \mathcal{L}_0 is performed at constant values of order parameters R . Additionally, the differentiation in \mathcal{L}_1 is performed at fixed values of Γ . Further details regarding the all-atom, multiscale analysis (AMA) for the Liouville equation can be found in [2], [3], [5], and [9]. The operators (10) and (11) differ from that of the previously mentioned papers [2] and [3] since in that work the conjugate momentum Π is treated as an order parameter. In the work that follows in this section, we treat this momentum term as a micro-variable instead.

Assuming the net force on the nanoparticle does not experience cancelation due to fluctuating terms, it can be written in terms of the individual atomic forces as

$$f = \sum_{i=1}^N F_i \theta_i. \quad (12)$$

We let $V(\Gamma_r)$ be the N -atom potential so that $\frac{\partial V}{\partial r_i} = -F_i$ for every $i = 1, \dots, N$. Next, we assume that ρ may be expressed as a power series in ϵ :

$$\rho = \sum_{n=0}^{\infty} \rho_n \epsilon^n \quad (13)$$

A set of time variables, defined via $t_n = \epsilon^n t$, is introduced to capture effects of processes occurring on the various timescales. The chain rule implies

$$\frac{\partial}{\partial t} = \sum_{n=0}^{\infty} \epsilon^n \frac{\partial}{\partial t_n}. \quad (14)$$

We then expand (9) using (13) and (14) and separate ϵ scales. Define for $n \in \{0\} \cup \mathbb{N}$,

$$\Lambda_n = \frac{\partial}{\partial t_n} - \mathcal{L}_n \quad (15)$$

where we take $\mathcal{L}_n = 0$ for $n > 1$. The expansion yields the equations

$$\Lambda_0 \rho_0 = 0,$$

and for $n \in \mathbb{N}$,

$$\Lambda_0 \rho_n = - \sum_{i=1}^n \Lambda_i \rho_{n-i}.$$

Assuming the statistical state of the system has quasi-equilibrium character, the lowest order distribution ρ_0 is taken to be independent of t_0 . Thus, to lowest order we find

$$\mathcal{L}_0 \rho_0 = 0. \quad (16)$$

This implies ρ_0 is a function of the conserved dynamical variables, notably the total energy H , as well as of R . The latter occurs because the derivatives $\frac{\partial}{\partial r_i}$ and $\frac{\partial}{\partial p_i}$ in \mathcal{L}_0 are to be taken at constant R , and thus $\mathcal{L}_0 R = 0$. Then, we can define

$$H = \sum_{i=1}^N \left(\frac{p_i^2}{2m_i} + V(\Gamma_r) \right)$$

and notice that $\mathcal{L}_0 H = 0$.

Using the entropy maximization principle, one arrives at the nanocanonical solution to (16) from [2]:

$$\rho_0 = \frac{e^{-\beta H} W(R, \underline{t})}{Q} \equiv \hat{\rho} W, \quad (17)$$

where

$$Q(\beta, R) = \int \Delta(\Gamma_r^*, R) e^{-\beta H^*} d\Gamma^*. \quad (18)$$

Here Δ is defined as in (6) and H^* is the Γ^* -dependent value of H . For convenience we write \underline{t} for the collection of slow time variables $\underline{t} = \{t_1, t_2, \dots\}$. As is standard in multiscale theory, determination of W is delayed until higher orders in the analysis. With this, ρ_0 is seen to factorize into the conditional probability $\hat{\rho}$ (i.e. for Γ given

R), multiplied by the reduced probability W for the slowly evolving state of the order parameter R . We define the thermal average of a given dynamical variable, $A(\Gamma)$ by

$$A^{th} \equiv \int \hat{\rho} \Delta A(\Gamma^*) d\Gamma^*. \quad (19)$$

Now, we will assume that the nancanonical ensemble obeys the Gibbs hypothesized equivalence between the long-time and ensemble averages. More specifically, we utilize a classical theorem of Birkhoff ([4] can provide more detail) which states that the thermal average of a dynamical variable $A(\Gamma)$ and its long-time average are equal. Using classical semigroup methods from applied partial differential equations (see [8] for more detail), one may show that the linear operator \mathcal{L}_0 is the infinitesimal generator of a strongly continuous semigroup on the function space $L^2(\Gamma)$. This semigroup is then well-defined and denoted by $e^{\mathcal{L}_0 t_0}$. Hence, in the analysis that follows, we will rely extensively on the property :

$$\lim_{t \rightarrow \infty} \frac{1}{t} \int_{-t}^0 e^{-\mathcal{L}_0 s} A ds = A^{th} \quad (20)$$

for all dynamical variables $A(\Gamma)$. Thus, the long-time average or time evolution of a variable does not affect the value of its thermal average as defined in (19). The survey [4] or the classic article [1] can provide more background information and detail from an ergodic theory perspective.

To $O(\epsilon)$ one finds

$$\Lambda_0 \rho_1 = -\Lambda_1 \rho_0. \quad (21)$$

Using the previously constructed semigroup $e^{\mathcal{L}_0 t_0}$, equation (21) admits the solution

$$\begin{aligned} \rho_1 &= e^{\mathcal{L}_0 t_0} \bar{A}_1 - \int_0^{t_0} e^{\mathcal{L}_0(t_0-t'_0)} \Lambda_1 \rho_0 dt'_0 \\ &= e^{\mathcal{L}_0 t_0} \bar{A}_1 - \int_0^{t_0} e^{\mathcal{L}_0(t_0-t'_0)} \left[\hat{\rho} \frac{\partial W}{\partial t_1} + \frac{P}{\hat{m}} \hat{\rho} \cdot \frac{\partial W}{\partial R} + \frac{P}{\hat{m}} \cdot \frac{\partial \hat{\rho}}{\partial R} W \right] dt'_0 \end{aligned}$$

The first order initial condition \bar{A}_1 is, for now, undetermined and has the dependence $\bar{A}_1(\Gamma, R, \underline{t})$. As a consequence of the cross-level communication inherent to multiscale analysis, the behavior of ρ_1 at large t_0 provides information about the t_1 -dependence of W , while the analysis of (7) provides a necessary condition on \bar{A}_1 that ensures the equation determining \widetilde{W} is closed. Letting $s = t'_0 - t_0$, one obtains

$$\rho_1 = e^{\mathcal{L}_0 t_0} \bar{A}_1 - t_0 \hat{\rho} \frac{\partial W}{\partial t_1} + \hat{\rho} \left[\beta f^{th} W - \frac{\partial W}{\partial R} \right] \cdot \int_{-t_0}^0 e^{-\mathcal{L}_0 s} \frac{P}{\hat{m}} ds. \quad (22)$$

In this equation, $\beta f^{th} = \frac{\partial}{\partial R} (\ln Q)$, so that f^{th} is the force averaged via the nancanonical ensemble. This term occurs because of the dependence of $\hat{\rho}$ on R and we will

verify the expression for $\frac{\partial \hat{\rho}}{\partial R}$ in the Appendix. Thus, using the Gibbs Hypothesis (20), we find

$$f^{th} = \lim_{t_0 \rightarrow \infty} \frac{1}{t_0} \int_{-t_0}^0 e^{-\mathcal{L}_0 s} f ds. \quad (23)$$

Next, we remove secular behavior from the t_0 -dependence in ρ_1 , thereby imposing the additional condition that ρ_1 remains bounded as $t_0 \rightarrow \infty$. Using (22), it can be seen that if ρ_1 grows in t_0 , it must do so at least linearly. Hence, we may ensure that ρ_1 does not grow in t_0 by requiring that $\lim_{t_0 \rightarrow \infty} \frac{1}{t_0} \rho_1 = 0$. We then divide by t_0 , take the limit as $t_0 \rightarrow \infty$ in equation (22), and use (20). Notice that $(P)^{th} = 0$, as it involves terms of the form $\int p_i \exp\left(\frac{p_i^2}{2m_i}\right) dp_i$. Assuming the first order initial data is taken in the nullspace of \mathcal{L}_0 , that is $\mathcal{L}_0 \overline{A}_1 = 0$, use of (20) yields

$$\lim_{t_0 \rightarrow \infty} \frac{\rho_1}{t_0} = -\frac{\partial W}{\partial t_1}.$$

Hence, we find

$$\frac{\partial W}{\partial t_1} = 0 \quad (24)$$

and the reduced probability density W is independent of t_1 . Note that this property follows regardless of the choice of \overline{A}_1 in the nullspace of \mathcal{L}_0 . Using this in (22), we find

$$\rho_1 = \overline{A}_1 + \hat{\rho} \left[\beta f^{th} W - \frac{\partial W}{\partial R} \right] \int_{-t_0}^0 e^{-\mathcal{L}_0 s} \frac{P}{\hat{m}} ds \quad (25)$$

concluding the $O(\epsilon)$ analysis, although \overline{A}_1 and W are not yet determined.

At this point, one would expect to conduct a $O(\epsilon^2)$ analysis of the problem and determine an equation for $\frac{\partial W}{\partial t_2}$. However, this is unnecessary as the correction to the reduced probability density depends only on ρ_0 and ρ_1 up to $O(\epsilon^2)$. Instead, define for all $n = 0, 1, 2, \dots$

$$\widetilde{W}_n(R, t) = \int \Delta(\Gamma_r^*, R) \rho_n(\Gamma^*, t) d\Gamma^* \quad (26)$$

so that, using (5) and (13), we may write

$$\widetilde{W} = \sum_{n=0}^{\infty} \epsilon^n \widetilde{W}_n. \quad (27)$$

Hence, we expand \widetilde{W} and ρ in powers of ϵ as in (13) and (27). Using (17) and (19),

the lowest order correction, \widetilde{W}_0 , can be calculated as

$$\begin{aligned}\widetilde{W}_0 &= \int \Delta(\Gamma_r^*, R) \rho_0(\Gamma^*, \underline{t}) d\Gamma^* \\ &= \int \Delta \rho_0(\Gamma^*, \underline{t}, R^*) d\Gamma^* \\ &= \int \Delta \hat{\rho} W(R^*, \underline{t}) d\Gamma^* \\ &= W(R, \underline{t}).\end{aligned}$$

For $\epsilon \rightarrow 0$, one may see that $\widetilde{W} \rightarrow W$. Hence, as the long time scales tend to zero, the correction tends to the reduced probability density. The $O(\epsilon)$ correction can be determined using (20) and (25), so that

$$\begin{aligned}\widetilde{W}_1 &= \int \Delta \rho_1(\Gamma^*, t) d\Gamma^* \\ &= \int \Delta \left[\overline{A}_1 - \hat{\rho} \left(\frac{\partial W}{\partial R} - \beta f^{th} W \right) \cdot \int_{-t_0}^0 ds e^{-\mathcal{L}_0 s} \frac{P^*}{\widehat{m}} \right] d\Gamma^* \\ &= \int \Delta \overline{A}_1(\Gamma^*, R^*, t) d\Gamma^* - \int \Delta \hat{\rho} \left(\frac{\partial W}{\partial R} - \beta f^{th} W \right) \cdot \int_{-t_0}^0 e^{-\mathcal{L}_0 s} \frac{P^*}{\widehat{m}} ds d\Gamma^* \Big|_{R=R^*} \\ &= \int \Delta \overline{A}_1(\Gamma^*, R^*, t) d\Gamma^* + \left(\int \Delta \hat{\rho} \int_{-t_0}^0 e^{-\mathcal{L}_0 s} \frac{P^*}{\widehat{m}} ds d\Gamma^* \right) \cdot \left(-\frac{\partial W}{\partial R}(R, \underline{t}) + \beta f^{th} W(R, \underline{t}) \right) \\ &= \int \Delta \overline{A}_1(\Gamma^*, R^*, t) d\Gamma^* + \left[\int_{-t_0}^0 \left(e^{-\mathcal{L}_0 s} \frac{P}{\widehat{m}} \right)^{th} ds \right] \cdot \left(-\frac{\partial W}{\partial R} + \beta f^{th} W \right) \\ &= \int \Delta \overline{A}_1(\Gamma^*, R^*, t) d\Gamma^*.\end{aligned}$$

Now, we may write $\rho(\Gamma, t)$ in terms of its expansion up to $O(\epsilon)$. Using (17) and

(25) in the right side of (7), we find

$$\begin{aligned}
\int \Delta \frac{P^*}{\hat{m}} \rho(\Gamma^*, t) d\Gamma^* &= \int \Delta \frac{P^*}{\hat{m}} \rho(\Gamma^*, t, R^*) d\Gamma^* \\
&= \int \Delta \frac{P^*}{\hat{m}} (\rho_0 + \epsilon \rho_1) d\Gamma^* \\
&= \int \Delta \hat{\rho} \frac{P^*}{\hat{m}} W(R^*, t) d\Gamma^* + \epsilon \int \Delta \frac{P^*}{\hat{m}} \bar{A}_1(\Gamma^*, R^*, t) d\Gamma^* \\
&\quad + \epsilon \left[\int \Delta \hat{\rho} \frac{P^*}{\hat{m}} \int_{-t_0}^0 e^{-\mathcal{L}_0 s} \frac{P^*}{\hat{m}} ds \left(\beta f^{th} W(R^*, \underline{t}) - \frac{\partial W}{\partial R}(R^*, \underline{t}) \right) d\Gamma^* \right] \\
&= \left(\frac{P}{\hat{m}} \right)^{th} W(R, \underline{t}) + \epsilon \int \Delta \frac{P^*}{\hat{m}} \bar{A}_1(\Gamma^*, R^*, t) d\Gamma^* \\
&\quad + \epsilon \left(\frac{P^*}{\hat{m}} \cdot \int_{-t_0}^0 e^{-\mathcal{L}_0 s} \frac{P^*}{\hat{m}} ds \right)^{th} \left(\beta f^{th} W(R, \underline{t}) - \frac{\partial W}{\partial R}(R, \underline{t}) \right) \\
&= \epsilon \int d\Gamma^* \Delta \frac{P^*}{\hat{m}} \bar{A}_1(\Gamma^*, R^*, t) + \epsilon \frac{\gamma}{\hat{m}^2} \left(\beta f^{th} W(R, \underline{t}) - \frac{\partial W}{\partial R}(R, \underline{t}) \right)
\end{aligned}$$

where the diffusion coefficient is

$$\gamma = \int_{-t_0}^0 (P(0) \cdot P(s))^{th} ds \quad (28)$$

and we use the notation $P(s) = e^{-\mathcal{L}_0 s} P$. Thus, (7) becomes

$$\frac{\partial \widetilde{W}}{\partial t} = -\epsilon^2 \frac{\partial}{\partial R} \cdot \left(\int \Delta \frac{P^*}{\hat{m}} \bar{A}_1(\Gamma^*, R^*, t) d\Gamma^* \right) + \epsilon^2 \frac{\partial}{\partial R} \cdot \left[\frac{\gamma}{\hat{m}^2} \left(\frac{\partial W}{\partial R} - \beta f^{th} W \right) \right].$$

Using the expressions for \widetilde{W}_0 and \widetilde{W}_1 , we can expand the reduced probability density as $\widetilde{W} = \widetilde{W}_0 + \epsilon \widetilde{W}_1$. Then, isolating \widetilde{W}_k terms and imposing the condition that \bar{A}_1 must stay bounded for large R , we find that this equation is closed only if $\bar{A}_1 = 0$. Thus, up to $O(\epsilon^2)$, the conserved equation (7) becomes the Smoluchowski equation:

$$\frac{\partial \widetilde{W}}{\partial t} = \epsilon^2 \frac{\partial}{\partial R} \cdot \left[\frac{\gamma}{\hat{m}^2} \left(\frac{\partial}{\partial R} - \beta f^{th} \right) \widetilde{W} \right]. \quad (29)$$

Hence, in the case of fast-evolving momentum, due to P and f being $O(\epsilon^0)$, the resulting behavior of the reduced probability density is governed by the Smoluchowski equation (29). In the next section, we alter these assumptions on the behavior of nanoparticle momentum and determine the corresponding changes in the structure of the equation for \widetilde{W} .

3 Multiscale Analysis: Fokker-Planck Equation

In this section, we again use multiscale techniques to show that under similar circumstances, the correction to the reduced probability density, \widetilde{W} , satisfies a Fokker-Planck

equation. In this situation, the momentum is not considered an atomistic variable, but instead as an order parameter. Hence, we define Γ , m , R , and P as before, but reformulate the problem to allow for the differing behavior of this slowly-evolving quantity.

To begin the multiscale analysis, we again introduce a dimensionless scaling parameter ϵ in the mass terms by writing

$$\epsilon = \frac{\hat{m}}{m}, \quad (30)$$

where \hat{m} is the mass of a typical atom. In this section, however, the assumptions on the system of interest change. We are now interested in significant migration distances on the order of the nanoparticle diameter, which we take to be $O(\epsilon^{-\frac{1}{2}})$, and hence scale R to be $O(\epsilon^{-\frac{1}{2}})$. Additionally, under the assumption that the system is near equilibrium, the nanoparticle kinetic energy, $\frac{P^2}{2m}$ is $O(\epsilon^0)$. Using the mass ratio scaling, this implies that $P = O(\epsilon^{-\frac{1}{2}})$, as well. Finally, we assume that the net force on the nanoparticle is reduced due to cancelation of atomic contributions, thus causing the momentum to evolve slowly. Hence, f is assumed to be $O(\epsilon^{\frac{1}{2}})$. A more detailed description of these assumptions can be found in [3].

Under these considerations, define the scaled order parameters Φ and Π by

$$\Phi = \epsilon^{\frac{1}{2}} R \quad (31)$$

and

$$\Pi = \epsilon^{\frac{1}{2}} P \quad (32)$$

respectively. The scaled net force f can then be written in terms of the individual atomic forces as

$$f = \epsilon^{-\frac{1}{2}} \sum_{i=1}^N F_i \theta_i, \quad (33)$$

and we let $V(\Gamma_r)$ be the N -atom potential so that $\frac{\partial V}{\partial r_i} = -F_i$ for every $i = 1, \dots, N$.

Let us assume ρ satisfies the Liouville Equation (4) where we again consider F_i to be the force on atom i and t to be time. In addition, we denote the collection of all atomic positions by $\Gamma_r = \{r_1, \dots, r_N\}$. Given the probability density, $\rho(\Gamma, t)$, we define

$$\widetilde{W}(\Phi, \Pi, t) = \int \Delta(\Gamma^*, \Phi, \Pi) \rho(\Gamma^*, t) d\Gamma^*. \quad (34)$$

where

$$\Delta(\Gamma^*, \Phi, \Pi) = \delta(\Phi - \Phi^*) \delta(\Pi - \Pi^*), \quad (35)$$

and the terms

$$\Phi^* = \epsilon^{\frac{1}{2}} \sum_{i=1}^N \frac{m_i}{m} r_i^* \theta_i$$

and

$$\Pi^* = \epsilon^{\frac{1}{2}} \sum_{i=1}^N p_i^* \theta_i$$

are the Γ^* -dependent values of Φ and Π . Then, using the dependence of \widetilde{W} on ρ , a solution to the Liouville equation, we may show that \widetilde{W} must satisfy a conserved equation similar to that of the previous section. Since ρ satisfies (4), we find

$$\begin{aligned} \frac{\partial \widetilde{W}}{\partial t} &= \int \Delta \frac{\partial \rho}{\partial t}(\Gamma^*, t) d\Gamma^* \\ &= - \int \Delta \left(\sum_{i=1}^N \frac{p_i^*}{m_i} \cdot \frac{\partial \rho}{\partial r_i^*} + F_i \cdot \frac{\partial \rho}{\partial p_i^*} \right) d\Gamma^* \\ &= \int \rho \left(\sum_{i=1}^N \frac{p_i^*}{m_i} \cdot \frac{\partial \Delta}{\partial r_i^*} + F_i \cdot \frac{\partial \Delta}{\partial p_i^*} \right) d\Gamma^* \\ &= - \int \rho \left(\sum_{i=1}^N \frac{p_i^*}{m_i} \cdot \frac{\partial R^*}{\partial r_i^*} + F_i \cdot \frac{\partial R^*}{\partial p_i^*} \right) \epsilon^{\frac{1}{2}} \frac{\partial \Delta}{\partial \Phi} d\Gamma^* \\ &\quad - \int \rho \left(\sum_{i=1}^N \frac{p_i^*}{m_i} \cdot \frac{\partial P^*}{\partial r_i^*} + F_i \cdot \frac{\partial P^*}{\partial p_i^*} \right) \epsilon^{\frac{1}{2}} \frac{\partial \Delta}{\partial \Pi} d\Gamma^* \\ &= \epsilon^{\frac{1}{2}} \frac{\partial}{\partial \Phi} \left(\int \rho \Delta \mathcal{L} R^* d\Gamma^* \right) + \epsilon^{\frac{1}{2}} \frac{\partial}{\partial \Pi} \left(\int \rho \Delta \mathcal{L} P^* d\Gamma^* \right) \\ &= -\epsilon^{\frac{1}{2}} \frac{\partial}{\partial \Phi} \left(\int \rho \Delta \frac{P^*}{m} d\Gamma^* \right) - \epsilon^{\frac{1}{2}} \frac{\partial}{\partial \Pi} \left(\int \rho \Delta \sum_{i=1}^N F_i \theta_i d\Gamma^* \right) \end{aligned}$$

Thus, the reduced probability density, \widetilde{W} , satisfies

$$\frac{\partial \widetilde{W}}{\partial t} = -\epsilon \frac{\partial}{\partial \Phi} \left(\int \rho \Delta \frac{\Pi^*}{m} d\Gamma^* \right) - \epsilon \frac{\partial}{\partial \Pi} \left(\int \rho \Delta f d\Gamma^* \right) \quad (36)$$

which is in conservative form.

Next, we conduct a multiscale analysis in order to determine ρ up to $O(\epsilon)$. Similar to the previous section, the N-atom probability density, $\rho(\Gamma, t)$, is assumed to be expressed as a function of two additional arguments, $\Upsilon(\Gamma, t, \cdot, \cdot)$ in such a way that when the last two arguments are evaluated at Φ and Π , ρ is obtained, i.e $\rho(\Gamma, t) = \Upsilon(\Gamma, t, \Phi, \Pi)$. Instead of labeling this new function, we will just extend our previous notation and refer to it as $\rho(\Gamma, t, \Phi, \Pi)$.

We apply the Liouville operator to $\rho(\Gamma, t, \Phi, \Pi)$ and invoke the chain rule to find

$$\frac{\partial \rho}{\partial t} = -\mathcal{L}_0 \rho - \sum_{i=1}^N \frac{p_i}{m_i} \cdot \frac{d\Phi}{dr_i} \frac{\partial \rho}{\partial \Phi} - \sum_{i=1}^N F_i \cdot \frac{d\Pi}{dp_i} \frac{\partial \rho}{\partial \Pi}.$$

Using (31) and (32) this becomes

$$\frac{\partial \rho}{\partial t} = -\mathcal{L}_0 \rho - \epsilon^{\frac{1}{2}} \frac{P}{m} \frac{\partial \rho}{\partial \Phi} - \epsilon f \frac{\partial \rho}{\partial \Pi}. \quad (37)$$

Here, we are writing \mathcal{L}_0 instead of \mathcal{L} because these derivatives are taken at constant values of Φ and Π . By introducing (30) and (32) into (37), the Liouville equation (4) transforms into a multiscale equation as

$$\frac{\partial \rho}{\partial t} = (\mathcal{L}_0 + \epsilon \mathcal{L}_1) \rho \quad (38)$$

where

$$\mathcal{L}_0 = - \sum_{i=1}^N \left[\frac{p_i}{m_i} \cdot \frac{\partial}{\partial r_i} + F_i \cdot \frac{\partial}{\partial p_i} \right] \quad (39)$$

and

$$\mathcal{L}_1 = - \frac{\Pi}{\hat{m}} \cdot \frac{\partial}{\partial \Phi} - f \cdot \frac{\partial}{\partial \Pi}. \quad (40)$$

Again, it must be noted that \mathcal{L} and \mathcal{L}_0 , while seemingly exact in definition, differ because the differentiation in \mathcal{L}_0 is performed at constant values of order parameters Φ and Π . Additionally, the differentiation in \mathcal{L}_1 is performed at fixed values of Γ . Unlike the previous section, the operators (10) and (11) are now the same as that of the previously mentioned papers [2] and [3] since the conjugate momentum Π is formulated as an order parameter.

Next, we assume that ρ may be expressed as a power series in ϵ :

$$\rho = \sum_{n=0}^{\infty} \rho_n \epsilon^n \quad (41)$$

A set of time variables, defined via $t_n = \epsilon^n t$, is introduced to capture effects of processes occurring on the various timescales. The chain rule implies

$$\frac{\partial}{\partial t} = \sum_{n=0}^{\infty} \epsilon^n \frac{\partial}{\partial t_n}. \quad (42)$$

We then expand (38) using (41) and (42) and separate ϵ scales. Define for $n \in \{0\} \cup \mathbb{N}$,

$$\Lambda_n = \frac{\partial}{\partial t_n} - \mathcal{L}_n \quad (43)$$

where we take $\mathcal{L}_n = 0$ for $n > 1$. The expansion yields the equations

$$\Lambda_0 \rho_0 = 0,$$

and for $n \in \mathbb{N}$,

$$\Lambda_0 \rho_n = - \sum_{i=1}^n \Lambda_i \rho_{n-i}.$$

Assuming the statistical state of the system has quasi-equilibrium character, the lowest order distribution ρ_0 is taken to be independent of t_0 . Thus, to lowest order we find

$$\mathcal{L}_0 \rho_0 = 0. \quad (44)$$

This implies ρ_0 is a function of the conserved dynamical variables, notably the total energy H , as well as of Φ and Π . The latter occurs because the derivatives $\frac{\partial}{\partial r_i}$ and $\frac{\partial}{\partial p_i}$ in \mathcal{L}_0 are to be taken at constant Φ and Π , and thus $\mathcal{L}_0 \Phi = \mathcal{L}_0 \Pi = 0$. As before, we define

$$H = \sum_{i=1}^N \left(\frac{p_i^2}{2m_i} + V(\Gamma_r) \right)$$

and notice that $\mathcal{L}_0 H = 0$.

Using the entropy maximization principle and proceeding as in [2], one arrives at the nanocanonical solution to (44):

$$\rho_0 = \frac{e^{-\beta H} W(\Phi, \Pi, \underline{t})}{Q} \equiv \hat{\rho} W, \quad (45)$$

where

$$Q(\beta, \Phi, \Pi) = \int \Delta(\Gamma^*, \Phi, \Pi) e^{-\beta H^*} d\Gamma^*. \quad (46)$$

This form of the nanocanonical solution is slightly different from that of [2] since it was stated in that article that Q is independent of Π . We find that this is not the case and determine the exact manner in which the Π dependence can be computed in the Appendix. Here, Δ is defined as in (35) and H^* is the Γ^* -dependent value of H . We label \underline{t} as the collection of slow time variables $\underline{t} = \{t_1, t_2, \dots\}$. As before, we define the thermal average of a given dynamical variable, $A(\Gamma)$ by

$$A^{th} = \int \Delta \hat{\rho} A(\Gamma^*) d\Gamma^* \quad (47)$$

and use the Gibbs Hypothesis:

$$\lim_{t \rightarrow \infty} \frac{1}{t} \int_{-t}^0 e^{-\mathcal{L}_0 s} A ds = A^{th} \quad (48)$$

for all dynamical variables $A(\Gamma)$. Notice that the thermal average, and thus the statements (47) and (48), depend upon the new order parameter Π because of (35).

To $O(\epsilon)$ one finds

$$\Lambda_0 \rho_1 = -\Lambda_1 \rho_0 \quad (49)$$

and using the semigroup $e^{\mathcal{L}_0 t_0}$ defined in Section 2, this equation admits the solution

$$\begin{aligned}\rho_1 &= e^{\mathcal{L}_0 t_0} \bar{A}_1 - \int_0^{t_0} e^{\mathcal{L}_0(t_0-t'_0)} \Lambda_1 \rho_0 dt'_0 \\ &= e^{\mathcal{L}_0 t_0} \bar{A}_1 - \int_0^{t_0} e^{\mathcal{L}_0(t_0-t'_0)} \left[\hat{\rho} \frac{\partial W}{\partial t_1} + \frac{\Pi}{\hat{m}} \frac{\partial \hat{\rho}}{\partial \Phi} W + \frac{\Pi}{\hat{m}} \hat{\rho} \frac{\partial W}{\partial \Phi} + f \frac{\partial \hat{\rho}}{\partial \Pi} W + f \hat{\rho} \frac{\partial W}{\partial \Pi} \right] dt'_0 \\ &= e^{\mathcal{L}_0 t_0} \bar{A}_1 - \int_0^{t_0} e^{\mathcal{L}_0(t_0-t'_0)} \left[\hat{\rho} \frac{\partial W}{\partial t_1} - \frac{\Pi}{\hat{m}} \beta \hat{\rho} f^{th} W + \frac{\Pi}{\hat{m}} \hat{\rho} \frac{\partial W}{\partial \Phi} + \beta f \hat{\rho} \frac{\Pi}{\hat{m}} W + f \hat{\rho} \frac{\partial W}{\partial \Pi} \right] dt'_0\end{aligned}$$

where we have used the results

$$\frac{\partial \hat{\rho}}{\partial \Phi} = -\beta \hat{\rho} f^{th}$$

and

$$\frac{\partial \hat{\rho}}{\partial \Pi} = \beta \hat{\rho} \frac{\Pi}{\hat{m}}.$$

These derivatives will be verified in the Appendix. The first order initial condition \bar{A}_1 is, for now, undetermined and has the dependence $\bar{A}_1(\Gamma, \Phi, \Pi, \underline{t})$. As a consequence of the cross-level communication inherent to multiscale analysis, the behavior of ρ_1 at large t_0 provides information about the t_1 -dependence of W , while the analysis of (36) provides a necessary condition on \bar{A}_1 that ensures the equation determining \widetilde{W} is closed. Letting $s = t'_0 - t_0$, one obtains

$$\begin{aligned}\rho_1 &= e^{\mathcal{L}_0 t_0} \bar{A}_1 - t_0 \hat{\rho} \frac{\partial W}{\partial t_1} - \hat{\rho} \beta \frac{\Pi}{\hat{m}} W \cdot \int_{-t_0}^0 e^{-\mathcal{L}_0 s} (f - f^{th}) ds \\ &\quad - t_0 \hat{\rho} \frac{\Pi}{\hat{m}} \cdot \frac{\partial W}{\partial \Phi} - \hat{\rho} \frac{\partial W}{\partial \Pi} \cdot \int_{-t_0}^0 e^{-\mathcal{L}_0 s} f ds.\end{aligned}\tag{50}$$

Next, we remove secular behavior from the t_0 -dependence in ρ_1 . As before, we assume that ρ_1 remains bounded as $t_0 \rightarrow \infty$. Using (50), it can be seen that if ρ_1 grows in t_0 , it must do so at least linearly. Hence, we may ensure that ρ_1 does not grow in t_0 by requiring that $\lim_{t_0 \rightarrow \infty} \frac{1}{t_0} \rho_1 = 0$. We then divide by t_0 , take the limit as $t_0 \rightarrow \infty$ in the above equation, and use (48). Assuming the first order initial data is in the nullspace of \mathcal{L}_0 , this yields

$$\lim_{t_0 \rightarrow \infty} \frac{\rho_1}{t_0} = -\frac{\partial W}{\partial t_1} - \frac{\Pi}{\hat{m}} \cdot \frac{\partial W}{\partial \Phi} - f^{th} \cdot \frac{\partial W}{\partial \Pi}.$$

Hence, we find

$$\Lambda_1^{th} \equiv \frac{\partial W}{\partial t_1} + \frac{\Pi}{\hat{m}} \cdot \frac{\partial W}{\partial \Phi} + f^{th} \cdot \frac{\partial W}{\partial \Pi} = 0\tag{51}$$

and W satisfies a Liouville equation in (t_1, Φ, Π) space. Note that (51) follows regardless of the choice of \bar{A}_1 in the nullspace of \mathcal{L}_0 . Using this in (50), we find

$$\rho_1 = \bar{A}_1 - \hat{\rho} \left[\beta \frac{\Pi}{\hat{m}} W + \frac{\partial W}{\partial \Pi} \right] \int_{-t_0}^0 e^{-\mathcal{L}_0 s} (f - f^{th}) ds \quad (52)$$

concluding the $O(\epsilon)$ analysis, although \bar{A}_1 and W are not yet determined.

As before, the correction to the reduced probability density depends only on ρ_0 and ρ_1 up to $O(\epsilon^2)$. Hence, define for every $n = 0, 1, 2, \dots$

$$\widetilde{W}_n(\Phi, \Pi, t) = \int \Delta(\Gamma^*, \Phi, \Pi) \rho_n(\Gamma^*, t) d\Gamma^* \quad (53)$$

so that, using (34) and (41), we may write

$$\widetilde{W} = \sum_{n=0}^{\infty} \epsilon^n \widetilde{W}_n. \quad (54)$$

In addition, we may expand \widetilde{W} and ρ in powers of ϵ as in (41) and (54). Using (48), the lowest order correction, \widetilde{W}_0 , can be calculated as

$$\begin{aligned} \widetilde{W}_0 &= \int \Delta(\Gamma^*, \Phi, \Pi) \rho_0(\Gamma^*, \underline{t}) d\Gamma^* \\ &= \int \Delta \rho_0(\Gamma^*, \underline{t}, \Phi^*, \Pi^*) d\Gamma^* \\ &= \int \Delta \hat{\rho} W(\Phi^*, \Pi^*, \underline{t}) d\Gamma^* \\ &= W(\Phi, \Pi, \underline{t}). \end{aligned}$$

For $\epsilon \rightarrow 0$, one may see that $\widetilde{W} \rightarrow W$. Hence, as the long time scales tend to zero, the correction tends to the reduced probability density. The $O(\epsilon)$ correction can be determined using (47). Notice that (48) implies $(e^{-\mathcal{L}_0 \tau} A)^{th} = A^{th}$ for any finite value of $\tau \in \mathbb{R}$. Using this and (52), we find

$$\begin{aligned} \widetilde{W}_1 &= \int \Delta \rho_1(\Gamma^*, t) d\Gamma^* \\ &= \int \Delta \left[\bar{A}_1 - \hat{\rho} \left(\frac{\partial W}{\partial \Pi} + \beta \frac{\Pi^*}{\hat{m}} W \right) \cdot \int_{-t_0}^0 ds e^{-\mathcal{L}_0 s} (f - f^{th}) \right] d\Gamma^* \\ &= \int \Delta \bar{A}_1(\Gamma^*, \Phi^*, \Pi^*, t) d\Gamma^* \\ &\quad - \int \Delta \hat{\rho} \left(\frac{\partial W}{\partial \Pi} + \beta \frac{\Pi^*}{\hat{m}} W \right) \cdot \int_{-t_0}^0 e^{-\mathcal{L}_0 s} (f - f^{th}) ds d\Gamma^* \Big|_{(\Phi, \Pi) = (\Phi^*, \Pi^*)} \\ &= \int \Delta \bar{A}_1(\Gamma^*, \Phi^*, \Pi^*, t) d\Gamma^* - \left[\int \Delta \hat{\rho} \int_{-t_0}^0 e^{-\mathcal{L}_0 s} (f - f^{th}) ds d\Gamma^* \right] \cdot \left(\frac{\partial W}{\partial \Pi}(\Phi, t) + \beta \frac{\Pi}{\hat{m}} W(\Phi, t) \right) \\ &= \int \Delta \bar{A}_1(\Gamma^*, \Phi^*, \Pi^*, t) d\Gamma^* - \int_{-t_0}^0 (f(s) - f^{th})^{th} ds \cdot \left(\frac{\partial W}{\partial \Pi} + \beta \frac{\Pi}{\hat{m}} W \right) \\ &= \int \Delta \bar{A}_1(\Gamma^*, \Phi^*, \Pi^*, t) d\Gamma^* \end{aligned}$$

where we use the notation $f(s) = e^{-\mathcal{L}_0 s} f$. Now, we may write $\rho(\Gamma, t)$ in terms of its expansion up to $O(\epsilon)$. Using (45) and (52) in the first term on the right side of (36), we find

$$\begin{aligned}
\int \Delta \frac{\Pi^*}{\widehat{m}} \rho(\Gamma^*, t) d\Gamma^* &= \int \Delta \frac{\Pi^*}{\widehat{m}} \rho(\Gamma^*, t, \Phi^*, \Pi^*) d\Gamma^* \\
&= \int \Delta \frac{\Pi^*}{\widehat{m}} (\rho_0 + \epsilon \rho_1) d\Gamma^* \\
&= \int \Delta \hat{\rho} \frac{\Pi^*}{\widehat{m}} W(\Phi^*, \Pi^*, t) d\Gamma^* + \epsilon \int \Delta \frac{\Pi^*}{\widehat{m}} \bar{A}_1(\Gamma^*, \Phi^*, \Pi^*, t) d\Gamma^* \\
&\quad - \epsilon \left[\int \Delta \hat{\rho} \frac{\Pi^*}{\widehat{m}} \left(\beta \frac{\Pi^*}{\widehat{m}} W + \frac{\partial W}{\partial \Pi} \right) \cdot \int_{-t_0}^0 ds e^{-\mathcal{L}_0 s} (f - f^{th}) d\Gamma^* \right] \\
&= \frac{\Pi}{\widehat{m}} W(\Phi, \Pi, t) + \epsilon \frac{\Pi}{\widehat{m}} \int \Delta \bar{A}_1(\Gamma^*, \Phi^*, \Pi^*, t) d\Gamma^* \\
&\quad - \epsilon \frac{\Pi}{\widehat{m}} \left(\beta \frac{\Pi}{\widehat{m}} W + \frac{\partial W}{\partial \Pi} \right) \cdot \left(\int_{-t_0}^0 (f(s) - f^{th}) ds \right)^{th} \\
&= \frac{\Pi}{\widehat{m}} W(\Phi, \Pi, t) + \epsilon \frac{\Pi}{\widehat{m}} \int \Delta \bar{A}_1(\Gamma^*, \Phi^*, \Pi^*, t) d\Gamma^*.
\end{aligned}$$

Similarly, the second term on the right side of (7) becomes

$$\begin{aligned}
\int \Delta f \rho(\Gamma^*, t) d\Gamma^* &= \int \Delta f \rho(\Gamma^*, t, \Phi^*, \Pi^*) d\Gamma^* \\
&= \int \Delta f (\rho_0 + \epsilon \rho_1) d\Gamma^* \\
&= \int \Delta \hat{\rho} f W(\Phi^*, \Pi^*, \underline{t}) d\Gamma^* + \epsilon \int \Delta f \bar{A}_1(\Gamma^*, \Phi^*, \Pi^*, t) d\Gamma^* \\
&\quad - \epsilon \left[\int \Delta \hat{\rho} f \left(\beta \frac{\Pi^*}{\widehat{m}} W + \frac{\partial W}{\partial \Pi} \right) \cdot \int_{-t_0}^0 ds e^{-\mathcal{L}_0 s} (f - f^{th}) d\Gamma^* \right] \\
&= f^{th} W(\Phi, \Pi, \underline{t}) + \epsilon \int \Delta f \bar{A}_1(\Gamma^*, \Phi^*, \Pi^*, t) d\Gamma^* \\
&\quad - \epsilon \left(\beta \frac{\Pi}{\widehat{m}} W + \frac{\partial W}{\partial \Pi} \right) \left(\int_{-t_0}^0 f(0) \cdot (f(s) - f^{th}) ds \right)^{th} \\
&= f^{th} W(\Phi, \Pi, \underline{t}) + \epsilon \int \Delta f \bar{A}_1(\Gamma^*, \Phi^*, \Pi^*, t) d\Gamma^* - \epsilon \theta \left(\beta \frac{\Pi}{\widehat{m}} W + \frac{\partial W}{\partial \Pi} \right)
\end{aligned}$$

where

$$\theta = \int_{-t_0}^0 [(f(0) \cdot f(s))^{th} - f^{th} \cdot f^{th}] ds. \quad (55)$$

Thus, (36) becomes

$$\begin{aligned}
\frac{\partial \widetilde{W}}{\partial t} &= -\epsilon \frac{\partial}{\partial \Phi} \cdot \left(\frac{\Pi}{\widehat{m}} W(\Phi, \Pi, \underline{t}) \right) - \epsilon^2 \frac{\partial}{\partial \Phi} \cdot \left(\frac{\Pi}{\widehat{m}} \int \Delta \bar{A}_1(\Gamma^*, \Phi^*, \Pi^*, t) d\Gamma^* \right) \\
&\quad - \epsilon \frac{\partial}{\partial \Pi} \cdot (f^{th} W(\Phi, \Pi, \underline{t})) + \epsilon^2 \frac{\partial}{\partial \Pi} \cdot \left[- \int \Delta f \bar{A}_1(\Gamma^*, \Phi^*, \Pi^*, t) d\Gamma^* + \theta \left(\beta \frac{\Pi}{\widehat{m}} W + \frac{\partial W}{\partial \Pi} \right) \right].
\end{aligned}$$

Using the expressions for \widetilde{W}_0 and \widetilde{W}_1 , we can expand the reduced probability density as $\widetilde{W} = \widetilde{W}_0 + \epsilon \widetilde{W}_1$. Then, isolating \widetilde{W}_k terms and imposing the condition that \overline{A}_1 must stay bounded for large Φ and Π , we find that this equation is closed only if $\overline{A}_1 = 0$. Thus, up to $O(\epsilon^2)$, the conserved equation (36) becomes the Fokker-Planck equation:

$$\frac{\partial \widetilde{W}}{\partial t} = -\epsilon \frac{\partial}{\partial \Phi} \cdot \left(\frac{\Pi}{\hat{m}} \widetilde{W} \right) - \epsilon \frac{\partial}{\partial \Pi} \cdot \left(f^{th} \widetilde{W} \right) + \epsilon^2 \frac{\partial}{\partial \Pi} \cdot \left[\theta \left(\beta \frac{\Pi}{\hat{m}} + \frac{\partial}{\partial \Pi} \right) \widetilde{W} \right]. \quad (56)$$

Hence, under the assumption that momenta have (comparatively) large values and evolve slowly, i.e., $P = O(\epsilon^{-\frac{1}{2}})$ and $f = O(\epsilon^{\frac{1}{2}})$, the reduced probability density obeys a Fokker-Planck equation given by (56).

4 Appendix

We first verify the Φ derivative of $\hat{\rho}$ used in the derivation of both equations. In Section 2, the variable R is used instead of Φ (as order parameters are unscaled with respect to ϵ), but the statements that follow can be applied exactly to R in the same manner as Φ . We claim

$$\frac{\partial \hat{\rho}}{\partial \Phi} = -\beta \hat{\rho} f^{th}.$$

Using (17) or (45), we see that

$$\frac{\partial \hat{\rho}}{\partial \Phi} = -\frac{e^{-\beta H}}{Q^2} \frac{\partial Q}{\partial \Phi}.$$

Notice that $\frac{\partial}{\partial \Phi} (e^{-\beta H}) = 0$ since Φ derivatives are to be taken at constant values of Γ . Using (18) or (46), we see that

$$\begin{aligned} \frac{\partial Q}{\partial \Phi} &= \int \frac{\partial \Delta}{\partial \Phi} e^{-\beta H^*} d\Gamma^* \\ &= - \int \frac{\partial \Delta}{\partial \Phi^*} e^{-\beta H^*} d\Gamma^* \\ &= \epsilon^{-\frac{1}{2}} \int \Delta \frac{\partial}{\partial R^*} (e^{-\beta H^*}) d\Gamma^* \end{aligned}$$

Now, since this integration is performed over all values of Γ^* , and hence Γ^* is not fixed, the energy depends upon the center of mass through the potential function. Notice, we may calculate $\frac{\partial V}{\partial R}$ as V depends upon R implicitly in the following manner. For every $i = 1, \dots, N$, write the residual displacement of each atomic position as $r_i = \sigma_i + R\theta_i$. Here the N variables $\{R, \sigma_1, \dots, \sigma_{N-1}\}$ constitute a complete set of variables as we may write σ_N in terms of each of the other σ_i using the constraint

$$\sum_{i=1}^N \sigma_i \theta_i = 0,$$

which follows by the definition of the residual coordinates. This change of variables is just a set of linear functions with constant coefficients, hence the Jacobian is constant and

$$\frac{\partial V}{\partial R} = \sum_{i=1}^N \frac{\partial V}{\partial r_i} \theta_i = -\epsilon^{\frac{1}{2}} f.$$

Since the kinetic energy is independent of Γ_r , we find

$$\frac{\partial}{\partial R^*} (e^{-\beta H^*}) = -\beta e^{-\beta H^*} \frac{\partial V^*}{\partial R^*} = \beta \epsilon^{\frac{1}{2}} f^* e^{-\beta H^*}.$$

Using this, the derivative of Q becomes

$$\begin{aligned} \frac{\partial Q}{\partial \Phi} &= \epsilon^{-\frac{1}{2}} \int \Delta e^{-\beta H^*} \beta \epsilon^{\frac{1}{2}} f^* d\Gamma^* \\ &= \beta \int \Delta e^{-\beta H^*} f^* d\Gamma^*. \end{aligned}$$

Hence, using the modified Gibbs Hypotheses in either section (20) or (48), we find

$$\begin{aligned} \frac{\partial \hat{\rho}}{\partial \Phi} &= -\frac{e^{-\beta H}}{Q^2} \frac{\partial Q}{\partial \Phi} \\ &= -\hat{\rho} \left(\frac{1}{Q} \cdot \frac{\partial Q}{\partial \Phi} \right) \\ &= -\hat{\rho} \beta \int \frac{1}{Q} \Delta e^{-\beta H^*} f^* d\Gamma^* \\ &= -\beta \hat{\rho} \left(\int \Delta \hat{\rho} f^* d\Gamma^* \right) \\ &= -\beta \hat{\rho} f^{th} \end{aligned}$$

and the verification of this derivative is complete.

Next, we verify the Π derivative of $\hat{\rho}$ used in Section 3. We claim

$$\frac{\partial \hat{\rho}}{\partial \Pi} = \beta \hat{\rho} \frac{\Pi}{\hat{m}}.$$

First, we use (46) and rewrite Q in terms of its Π dependence using the Fourier transform. Since the potential and kinetic energies depend exclusively on r_i and p_i variables respectively, we separate Q into two different integrals involving these variables. In addition, we separate the momentum integrals into the momenta of particles in the host medium, denoted $\Gamma_0 = \{p_i : \theta_i = 0\}$ and those in the nanoparticle, denoted $\Gamma_1 = \{p_i : \theta_i = 1\}$. Using the notation

$$K_0 = \sum_{i=1}^N \frac{p_i^2}{2m_i} (1 - \theta_i)$$

and

$$K_1 = \sum_{i=1}^N \frac{p_i^2}{2m_i} \theta_i$$

for the kinetic energies of the host medium and nanoparticle, respectively, we write Q as

$$Q(\beta, \Phi, \Pi) = \left(\int \delta(\Phi - \Phi^*) e^{-\beta V^*} d\Gamma_r^* \right) \left(\int e^{-\beta K_0^*} d\Gamma_0^* \right) \left(\int \delta(\Pi - \Pi^*) e^{-\beta K_1^*} d\Gamma_1^* \right). \quad (57)$$

Keeping the Γ_r^* and Γ_0^* integrals as they are (notice further that the Γ_0^* integral is constant), we focus on the Γ_1^* integral. We may again split the Γ_1^* integral into one each in the x, y , and z directions. We will consider the integral in the x -direction, labeled I_x , and state that the results we obtain will follow for the integrals in the other directions in the same manner.

Now, we relabel the momenta in the nanoparticle, 1 through M , and write their x -coordinates as x_1 through x_M . Then, write the x -directional Dirac mass $\delta(\Pi_x - \Pi_x^*)$ using the Fourier transform of the function $f(k) = 1$ as

$$\delta(\Pi_x - \Pi_x^*) = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{\infty} \exp \left[ik \left(\Pi_x - \sqrt{\epsilon} \sum_{l=1}^M x_l \right) \right] dk.$$

Then, using the Inverse Fourier Transform on the resulting Gaussians

$$\exp(-\lambda k^2) = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{\infty} \frac{1}{\sqrt{4\pi\lambda}} \exp(-ikz) \exp\left(-\frac{z^2}{4\lambda}\right) dz.$$

and (30), we find

$$\begin{aligned} I_x &= \frac{1}{\sqrt{2\pi}} \int \int_{-\infty}^{\infty} \exp \left[ik \left(\Pi_x - \sqrt{\epsilon} \sum_{l=1}^M x_l \right) \right] dk \\ &\quad \cdot \exp\left(-\frac{\beta}{2m_1} x_1^2\right) \cdots \exp\left(-\frac{\beta}{2m_M} x_M^2\right) dx_1 \cdots dx_M \\ &= \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{\infty} \exp(ik\Pi_x) \left[\int \exp(-ik\sqrt{\epsilon}x_1) \exp\left(-\frac{\beta}{2m_1} x_1^2\right) dx_1 \right] \cdots \\ &\quad \left[\int \exp(-ik\sqrt{\epsilon}x_M) \exp\left(-\frac{\beta}{2m_M} x_M^2\right) dx_M \right] dk \\ &= \int_{-\infty}^{\infty} e^{ik\Pi_x} \left[\sqrt{\frac{m_1}{\beta}} e^{-\frac{\epsilon m_1 k^2}{2\beta}} \right] \cdots \left[\sqrt{\frac{m_M}{\beta}} e^{-\frac{\epsilon m_M k^2}{2\beta}} \right] dk \\ &= \sqrt{\frac{m_1}{2\pi\beta}} \cdots \sqrt{\frac{m_M}{2\pi\beta}} \int_{-\infty}^{\infty} \exp(ik\Pi_x) \exp\left[-\frac{\epsilon k^2}{2\beta} m\right] dk \\ &= C_1 \exp\left(-\frac{\beta}{2\hat{m}} \Pi_x^2\right) \end{aligned}$$

where

$$C_1 = \sqrt{\frac{m_1}{2\pi\beta}} \cdots \sqrt{\frac{m_M}{2\pi\beta}} \cdot \sqrt{\frac{2\pi\beta}{\hat{m}}}.$$

We extend this in the y and z directions and multiply to find

$$\int \delta(\Pi - \Pi^*) e^{-\beta K_1^*} d\Gamma_1^* = (C_1)^3 \exp\left(-\frac{\beta}{2\hat{m}}\Pi^2\right).$$

Thus, we can write

$$Q(\beta, \Phi, \Pi) = Q_1(\Phi)(C_1)^3 C_2 \exp\left(-\frac{\beta}{2\hat{m}}\Pi^2\right)$$

where

$$Q_1(\Phi) = \left(\int \delta(\Phi - \Phi^*) e^{-\beta V^*} d\Gamma_r^* \right)$$

and

$$C_2 = \left(\int e^{-\beta K_0^*} d\Gamma_0^* \right).$$

Finally, $\hat{\rho}$ can be expressed in the form

$$\hat{\rho} = \frac{e^{-\beta H}}{Q_1(\Phi)(C_1)^3 C_2} \exp\left(\frac{\beta}{2\hat{m}}\Pi^2\right). \quad (58)$$

Taking a Π derivative in (58), which must be done at fixed values of Γ , we find

$$\frac{\partial \hat{\rho}}{\partial \Pi} = \beta \hat{\rho} \frac{\Pi}{\hat{m}}$$

and the verification of this derivative is complete.

References

- [1] Hopf, E., Proof of Gibbs' Hypothesis on the Tendency Toward Statistical Equilibrium. *Proc. Natl. Acad. Sci. U. S. A.* **18**(4):333-340 (1932).
- [2] Miao, Y. and Ortoleva, P., All-atom multiscaling and new ensembles for dynamical nanoparticles. *J. Chem. Phys.*, **125** 044901 (2006).
- [3] Miao, Y. and Ortoleva, P., Viral structural transitions: An all-atom multiscale theory. *J. Chem. Phys.*, **125** 214901 (2006).
- [4] Oliveira, C. and Werlang, T., Ergodic hypothesis in classical statistical mechanics. *Revista Brasileira de Ensino de Fisica*, **29**(2):189-201 (2007).
- [5] Ortoleva, P., Nanoparticle Dynamics: A Multiscale Analysis of the Liouville Equation. *J Phys. Chem.*, **109** 21258 (2005).

- [6] Peters, M.H., *J. Chem. Phys.* **110** 528 (1998).
- [7] Peters, M.H., *J. Stat. Phys.* **94** 557 (1999).
- [8] Renardy, M. and Rogers, R., An Introduction to Partial Differential Equations. (2000)
- [9] Shreif, Z. and Ortoleva, P., Curvilinear All-Atom Multiscale (CAM) Theory of Macromolecular Dynamics, *J. Stat. Physics*, to appear (2007).
- [10] Shea, J.E. and Oppenheim, I., *J. Phys. Chem* **100** 19035 (1996).
- [11] Shea, J.E. and Oppenheim, I., *Physica A* **247** 417 (1997).